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Attorney Docket No. XTR004 CIP

Client/Matter No. 80148.0212.002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Gerdes et al.

Serial No. 09/944,604

Filed: August 31, 2001

For: NUCLEIC ACID ARCHIVING

Group Art Unit: 1634

Examiner: Ethan Whisenant

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11/4/02

**AMENDMENT UNDER 37 CFR § 1.111**  
**IN RESPONSE TO RESTRICTION REQUIREMENT**

To: BOX RESPONSE/FEE  
Commissioner for Patents  
Washington, D.C. 20231

Sir:

In response to the Office Action, Paper No. 6, mailed on August 27, 2002, please amend the above-identified application as follows:

IN THE CLAIMS:

Please cancel claims 1-142 according to the attached sheets.

Please add new claims 143-173 according to the attached sheets.

**REMARKS**

In an Office Action, Paper, No. 6, dated August 27, 2002, a restriction requirement was made by the Examiner to pending claims 1-142 in the above-referenced application. The claims were placed into eight groups: Group I (claims 1-18), drawn to a method of archiving nucleic acid; Group II (claims 19-37), drawn to a method of amplifying one or more target nucleic acids; Group III (claims 38-50), drawn to a method of purifying a nucleic acid present in a sample; Group IV (claims 51-60), drawn to a method of concentrating the nucleic acid present in a sample; Group V (claims 61-70) drawn to a method of capturing a target nucleic acid via hybridization; Group VI (claims 71-94), drawn to a method of coating the surface of a plastic material with a solid phase matrix; Group VII (claims 95-133) drawn to a method of coating the

surface of an oxide substrate with a solid phase matrix and the product made by said process; and Group VIII (claims 134-142), drawn to a kit for nucleic acid manipulation.

In response thereto, all pending claims 1-142 have been cancelled, and new claims 143-173, drawn to a method of manipulating a target nucleic acid contained in a sample, have been added. Support for new claims 143-173 can be found in the Specification in paragraphs [0012] – [0018], [0049]-[0050], [0053] – [0055], [0058], [0068], [0073] – [0074], [0085], [0091], [0093], and [0113].

It is believed that all the claims now pending in this patent application are allowable. Therefore, it is respectfully requested that the Examiner reconsider the claims and grant an early allowance. If any questions or issues remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number listed below. The fee required for filing a Petition for a one month time extension accompanies this Amendment. Should any additional fee be required, please charge Deposit Account No. 50-1123.

Respectfully submitted,

Oct. 25, 2002  
Date



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## MARKED UP VERSION OF CLAIMS

Please cancel pending claims 1-142 and add new claims 143-173.

143. (New) A method of manipulating a target nucleic acid contained in a sample, comprising:

- (a) providing a solid phase matrix, wherein said matrix is a specific binding material having one or more electropositive materials rendered hydrophilic; and
- (b) flowing said sample through or over said solid phase matrix, wherein said nucleic acid becomes tightly bound to said solid phase matrix.

144. (New) The method of claim 143, wherein said sample is flowed over said matrix at a rate between about 0.5 mL/min and 2mL/min.

145. (New) The method of claim 143, wherein step (a) further comprises:

(i) contacting a probe comprising a nucleic acid sequence that is complementary to a specific sequence of said target nucleic acid with said solid phase matrix under conditions that allow said probe to become tightly bound to said matrix, and wherein during step (b) said sample is flowed through or over said solid phase matrix under conditions that allow said target nucleic acid to hybridize to said probe to form a complex.

146. (New) The method of claim 143, wherein said sample contains non-nucleic acid contaminants and said method further comprises:

(c) washing said matrix-bound nucleic acid one or more times with a wash buffer to remove said non-nucleic acid contaminants to provide a purified nucleic acid tightly bound to said matrix.

147. (New) The method of claim 146, wherein said wash buffer is selected from the group consisting of water, 70% ethanol, polymerase chain reaction buffer, TRIS buffer, EDTA buffer, lithium chloride, and guanidium detergent based buffer.

148. (New) The method of claim 146, further comprising:

(d) incubating said matrix-bound purified nucleic acid in a displacement buffer, wherein a small amount of said purified nucleic acid is displaced from said matrix into said displacement buffer; and

(e) amplifying one or more target nucleic acid sequences of said displaced purified nucleic acid.

149. (New) The method of claim 148, wherein said displacement buffer is Tris/HCl buffer or water.

150. (New) The method of claim 148, further comprising repeating steps (d) and (e) one or more times.

151. (New) The method of claim 143, further comprising:

(c) contacting said matrix-bound target nucleic acid with a set of primer nucleic acid sequences and a buffer that allows said primer sequences to hybridize to said matrix-bound target nucleic acid; and

(d) amplifying said target nucleic acid to produce an amplified reaction mixture, wherein said target nucleic acid sequence remains tightly bound to said matrix.

152. (New) The method of claim 151, wherein said amplification methodology is selected from the group consisting of PCR, SDA, NASBA, IsoCR, CRCA, Q beta replicase, branched chain DNA, RT-PCR, and unwinding coil amplification.

153. (New) The method of claim 151, further comprising repeating steps (c) and (d) one or more times.

154. (New) The method of claim 151, wherein said sample comprises two or more target nucleic acids and said two or more target nucleic acids are amplified in series.

155. (New) The method of claim 151, wherein said target nucleic acid contains multiple target nucleic acid sequences, said method further comprising contacting said matrix-bound target nucleic acid in step (c) with multiple primer sets to pre-amplify said multiple target sequences, wherein said multiple target sequences are amplified simultaneously.

156. (New) The method of claim 155 wherein step (c) further comprises dividing said pre-amplified reaction mixture into a plurality of aliquots and adding at least one of said primer sets to each of said aliquots, wherein each of said aliquots is amplified according to step (d).

157. (New) The method of claim 143, wherein said electropositive material comprises an element selected from the group consisting of aluminum, titanium, zirconium, hafnium, scandium, yttrium, lanthanum, vanadium, tantalum, chromium, molybdenum, tungsten, boron, gallium, indium, germanium, tin, and lead.

158. (New) The method of claim 143, wherein said matrix is selected from the group consisting of alpha aluminum oxide, gamma aluminum oxide and an aluminum oxide thin-film of mixed composition.

159. (New) The method of claim 143, wherein said matrix is  $Ti_2O_3$ .

160. (New) The method of claim 143, wherein said matrix is modified ZrO<sub>2</sub>.
161. (New) The method of claim 143, wherein said nucleic acid is selected from the group consisting of double stranded DNA, single stranded DNA, RNA, or PNA.
162. (New) The method of claim 143, wherein said nucleic acid is double stranded DNA, and step (b) further comprises adding a buffer that allows said DNA to be bound to said matrix as single stranded DNA.
163. (New) The method of claim 162, wherein said buffer is selected from the group consisting of guanidine thiocyanate-based buffers, alkaline buffers, lithium chloride, and detergent based buffers.
164. (New) The method of claim 143 wherein said sample contains both DNA and RNA, and step (b) is performed under conditions wherein said matrix exclusively binds said DNA.
165. (New) The method of claim 164, wherein said conditions comprise adding to said sample a buffer selected from the group consisting of guanidine thiocyanate-based buffers, alkaline buffers, lithium chloride, and detergent based buffers prior to contacting said sample with said solid phase matrix.
166. (New) The method of claim 164, wherein said conditions comprise adding to said solid phase matrix a buffer selected from the group consisting of guanidine thiocyanate-based buffers, alkaline buffers, lithium chloride, and detergent based buffers prior to contacting said sample with said solid phase matrix.
167. (New) The method of claim 143, wherein said sample contains both DNA and RNA, and step (b) is performed under conditions wherein said matrix exclusively binds said RNA.
168. (New) The method of claim 167, wherein said conditions comprise adding a DNA degrading reagent to said sample prior to contacting said sample with said solid phase matrix.
169. (New) The method of claim 168, wherein said DNA degrading reagent is DNase.
170. (New) The method of claim 143, wherein said sample comprises blood, stool, sputum, mucus, cervical fluid, vaginal fluid, cerebral spinal fluid, serum, urine, saliva, teardrop, biopsy samples, histological tissues, tissue culture products, bacterial cultures, swabs, agricultural products, environmental samples, waste water, drinking water, foodstuff, or air.
171. (New) The method of claim 143, wherein said solid phase matrix is coated on the surface of a substrate.
172. (New) The method of claim 171, wherein said substrate is a glass or polymeric

material.

173. (New) The method of claim 171, wherein said substrate is in the shape of tubes, plates, membranes, capillaries, slides, beads, microparticles, fibers, microchannels, and microarrays.

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